REMARKS

Claims 12-19 were pending in this application when last examined. Claims 16-19 have been withdrawn.

Claim 12 has been amended. Support for amended claim 12 can be found in original claim 16. No new matter has been added.

CLAIM REJECTION - 35 USC § 102(b)

At page 2, item 4, the Office Action rejects claims 12-15 under 35 U.S.C. § 102(b) as being anticipated by BIANCHI et al. (WO 2002/074337). Applicants respectfully traverse the rejection.

Claim 12 is directed to a method for treating vascular diseases related to endothelial and smooth muscle cells proliferation comprising administering to a subject in need thereof a therapeutic agent comprising a therapeutically active amount of an HMG box binding molecule. BIANCHI fails to teach or suggest such a method.

BIANCHI describes HMGB1 as a chemoattractant that causes cell shape changes and cytoskeleton reorganization and induces the migration cells, such as smooth muscle cells and fibroblasts (*see*, page 1, lines 10-13, and page 5, lines 18-22). BIANCHI, however, fails to teach or suggest that an HMG box protein could play any role in cell proliferation.

The instant specification discloses, beginning at page 2, that HMGB1 induces endothelial and smooth muscle cell proliferation. Figure 1 illustrates the results of *in vitro* cell proliferation experiments which demonstrate that HMGB1 caused aorta endothelial cells and smooth muscle cells to divide and proliferate. Furthermore, antibodies against HMGB1 abolished the effect of HMGB1 (*see*, page 3, lines 17-18). Also of note, while HMGB1 was known to be a chemoattractant for fibroblasts, HMGB1 had no effect on fibroblast proliferation (*see*, page 3, lines 19-21).

Applicants further disclose that molecules which modulate or block the interaction between HMGB1 and its receptor (RAGE) can be used in a pharmacological preparation for the treatment of diseases related to endothelial and/or smooth muscle cell proliferation, e.g., events that occur after coronary and/or carotid angioplasty, angiographic surgery and surgery using catheters (*see*, page 4, lines 1-8).

BIANCHI fails to teach or suggest that HMGB1 protein would have any effect on cell proliferation, and more specifically, endothelial or smooth muscle cell proliferation. In distinction from the chemoattractant properties disclosed in BIANCHI, instant claim 12 is directed to a method for treating vascular diseases related to endothelial and smooth muscle cells proliferation. The method includes administering

to a subject a therapeutically active amount of an HMG box binding molecule, e.g., an antibody against HMGB1.

For at least these reasons, BIANCHI fails to teach or suggest, and fails to anticipate, claim 12 and claims 13-15 dependent thereon. Accordingly, Applicants request reconsideration and withdrawal of the rejection.

NONSTATUTORY OBVIOUSNESS-TYPE DOUBLE PATENTING

At page 3, item 6, the Office Action provisionally rejects claims 12-15 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10, 26 and 29 of copending Application No. 10/471641 (US 2004/0136979). Applicants respectfully traverse the rejection.

Regarding Application No. 10/471641, claim 10 as amended is presently directed to a method of treating arterial stenosis or restenosis in an individual, comprising administering to an individual at risk of developing or having arterial stenosis or restenosis a molecule that blocks interaction of an HMGB1 protein on its receptors, wherein the molecule is selected from the group consisting of an antibody against HMGB1 or a four way DNA. Claims 26 and 29 depend from claim 10. These claims would not have rendered the instant claims 12-15 obvious to one of ordinary skill in the art.

As detailed in the above remarks, claim 12 is directed to a method for treating vascular diseases related to endothelial and smooth muscle cells proliferation. This stands in distinction from treating arterial stenosis or restenosis. Stenosis or restenosis is an abnormal narrowing in a blood vessel (or other tubular organ or structure. There are many potential causes of stenosis and restinosis such as birth defects, infection, inflammation, ischemia, neoplasia and atherosclerosis. Thus, treating arterial stenosis or restinosis does not render obvious the treatment of other vascular diseases related to cell proliferation.

For at least these reasons, claims 1, 26 and 29 of Application No. 10/471641 would not have rendered obvious instant claims 12-15. Accordingly, Applicants request reconsideration and withdrawal of the rejection.

CLAIM REJECTION - 35 USC § 102(e)

At page 4, item 10, the Office Action rejects claims 12-15 under 35 U.S.C. § 102(e) as being anticipated by copending Application No. 10/471641 (US 2004/0136979). Applicants respectfully traverse the rejection.

As detailed in the above remarks regarding the nonstatutory obviousness-type double patenting rejection, US 2004/0136979 relates to a method of treating arterial stenosis or restenosis in an individual that includes administering a

molecule to block the interaction of HMGB1 protein on its receptors. US 2004/0136979, however, fails to teach or suggest a method for treating vascular diseases related to endothelial and smooth muscle cells proliferation, as featured in instant claims 12-15.

Claim 12 is directed to a method for treating vascular diseases related to endothelial and smooth muscle cells proliferation comprising administering to a subject a therapeutically active amount of an HMG box binding molecule. In contrast, US 2004/0136979 describes treating stenosis or restenosis, which is an abnormal narrowing in a blood vessel that does not involve cell proliferation. Furthermore, US 2004/0136979 fails to teach or suggest that an HMG box protein could play any role in cell proliferation.

For at least these reasons, US 2004/0136979 fails to teach or suggest, and fails to anticipate, claim 12 and claims 13-15 dependent thereon. Accordingly, Applicants request reconsideration and withdrawal of the rejection.

CONCLUSION

Entry of the above amendments is earnestly solicited. Applicants respectfully request that a timely Notice of Allowance be issued in this case.

Should there be any matters that need to be resolved in the present application the Examiner is respectfully

requested to contact the undersigned at the telephone number listed below.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,
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